

## 9

## EXAMPLE 9 (Hard gelatin capsule)

Cyclosporin	50 mg
Poloxamer 188	300 mg
Sorbitol	350 mg
Total	700 mg

The above-mentioned components were treated according to the same procedure as Example 1 to obtain the powder which was then filled in a hard gelatin capsule to obtain the capsule preparation.

## EXAMPLE 10 (Hard gelatin capsule)

Cyclosporin	50 mg
Solutol HS15	150 mg
Cremophor RH60	200 mg
Sorbitol	350 mg
Aerosil 200	17 mg
Total	767 mg

Cyclosporin, Solutol HS15, Cremophor RH60 and sorbitol were treated according to the same procedure as Example 1 to obtain the powder which was then mixed with Aerosil 200. The mixture was filled in a hard gelatin capsule to obtain the capsule preparation.

## TEST EXAMPLE

Comparative test for bioavailability of the composition of the present invention and the commercial product in dogs

The bioavailability of the composition according to the present invention was identified from the following experiment.

## a) Test compositions

Composition I (composition of the present invention):

Cyclosporin	25 mg
Solutol HS15	250 mg
Sylsilia 50	125 mg
Collidon CL	8 mg
Total	408 mg

Composition II: SANDIMUN<sup>®</sup> 25 mg Soft capsule (Lot No. 114MFD1293)

## b) Test procedure

In this experiment, 6 male dogs weighing 11.0–15.0 kg were used as the test animal. The test animal was fasted from 18 hours before administration of the test compositions, except that they are allowed to drink water. The test compositions (4 capsules) corresponding to 100 mg of cyclosporin per dog was orally administered by compulsion to the test animal and then 50 ml of water was administered to each test animal. After 4 hours from administration of the test compositions the foodstuffs were administered to the test animal. In this test the test animals were divided into two groups in which each group consists of 3 dogs, and the experiment was practiced according to the cross-over test method.

Blood was collected from a juglar vein in an amount of 2 ml each time before administration of the test compositions and 1, 1.5, 2, 2.5, 3, 3.5, 4, 5, 6, 8, 10 and 12 hours after

## 10

administration of the test compositions, and then stored at  $-18^{\circ}\text{C}$ . According to a method disclosed in the literature (Pharmaceutical Research, Vol. 8, No. 4, 1991, p518), the blood was pretreated with an organic solvent and then analyzed by means of HPLC [solvent:  $\text{CH}_3\text{CN}/\text{pH}$  2.5 buffer solution/methanol=50/45/5, column: Lichrosorb RP-8 (5  $\mu\text{m}$ ), wavelength: 215 nm, temperature:  $70^{\circ}\text{C}$ ., flow rate: 2.0 ml/min.].

## C) Result

As the result of administration of two test compositions to 6 dogs according to the above-mentioned test procedure, AUC (ng.hr/ml) and blood concentration of cyclosporin in each group were described in the following Tables 1 and 2 and also depicted in FIG. 1.

TABLE 1

AUC (ng · hr/ml) after oral administration of the composition of the present invention and the commercial product		
	Composition I	Composition II
A	3305.05	3016.43
B	3487.46	2910.20
C	2979.27	1614.13
D	6948.64	3244.72
E	3448.35	2354.94
F	6358.45	3166.61
Average	4421.20	2717.84

TABLE 2

Blood concentration (ng/ml) of cyclosporin after oral administration of the composition of the present invention and the commercial product		
Time (hr)	Composition I	Composition II
0.0	0.00	0.00
1.0	546.96	629.12
1.5	617.35	759.46
2.0	1013.82	399.60
2.5	668.41	369.04
3.0	592.74	254.22
4.0	421.03	228.50
5.0	317.38	167.87
6.0	275.43	167.63
8.0	187.99	148.06
10.0	185.46	124.81
12.0	130.73	97.75

As can be seen from the result shown in the above tables and figure, the composition of the present invention shows an increase in the bioavailability by about 62% in comparison with the composition II as the commercial product. In addition, in view of the fact that the blood concentration of cyclosporin is maintained at 250 ng/ml or more by administration of the composition of the present invention, the duration of an effective blood concentration of about 250 ng/ml following to administration of the composition of the present invention is about two times that of the commercial product.

Although this invention has been described in its preferred form with a certain degree of particularity, it is appreciated by those skilled in the art that the present disclosure of the preferred form has been made only by way of example and that numerous changes in the details of the construction, combination and arrangement of parts may be resorted to without departing from the spirit and scope of the invention.

What is claimed is:

1. A cyclosporin-containing powder composition which comprises